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Rifaximin Significantly Improves Bowel Movement Urgency in Patients With Irritable Bowel Syndrome With Diarrhea: A Pooled Analysis of Three Phase 3 Trials

Philip S. Schoenfeld, MD[1]; Darren M. Brenner, MD[2]; Nipaporn Pichetshote, MD[3]; Zeev Heimanson, PharmD[4]; Brian E. Lacy, PhD, MD[5]

[1]John D. Dingell VA Medical Center, Detroit, MI; [2]Feinberg School of Medicine, Northwestern University, Chicago, IL; [3]Cedars-Sinai Medical Center, Los Angeles, CA; [4]Salix Pharmaceuticals, Bridgewater, NJ; [5]Mayo Clinic, Jacksonville, FL

BACKGROUND

- Rifaximin is a nonsystemic antibiotic indicated in the United States for the treatment of adults with irritable bowel syndrome with diarrhea (IBS-D)[1] and has been shown to improve multiple IBS-D symptoms, including abdominal pain, bloating, and stool consistency[2,3]
- Bowel movement (BM) urgency is a common symptom in IBS,[4] and the degree of urgency is associated with decreased quality of life[5,6]

AIM

- To assess improvements in BM urgency after 2 weeks of treatment with rifaximin in patients with IBS-D

METHODS

- Data were pooled post hoc from 2 identically designed, phase 3, randomized, double-blind, placebo-controlled trials (TARGET 1 and 2) and the initial, open-label period of a third phase 3 trial (TARGET 3; Table 1)[2,3]
- Adults with IBS-D (Rome II[2]/III[3] diagnostic criteria) were treated with placebo or rifaximin 550 mg three times daily (TID) for 2 weeks, followed by a 4-week treatment-free period to evaluate response; total treatment-free follow-up period was 10 weeks

Table 1. Phase 3 Clinical Studies*

Study	Study Design	Trial Registration	Treatment
Study 1 (TARGET 1)[2]	R, PBO	NCT00731679	Rifaximin 550 mg or placebo TID for 2 weeks
Study 2 (TARGET 2)[2]	R, PBO	NCT00724126	Rifaximin 550 mg or placebo TID for 2 weeks
Study 3 (TARGET 3 OL Phase)[3]	OL	NCT01543178	Rifaximin 550 mg TID for 2 weeks

*Although TARGET 1 and TARGET 2 could enroll patients with any form of non-constipation IBS (based on Rome II diagnostic criteria), all of the patients enrolled had IBS-D.[2,7]
OL = open label; PBO = placebo-controlled; R = randomized; TARGET = Targeted, Nonsystemic Antibiotic Rifaximin Gut-Selective Evaluation of Treatment for IBS-D; TID = 3 times daily.

- Daily BM urgency was determined by a yes/no response by patients to the question "Have you felt or experienced a sense of urgency today?" in TARGET 1 and 2, or "Have you felt or experienced a sense of urgency in the last 24 hours with any of your bowel movements?" in TARGET 3
- BM urgency response was defined as a ≥30% reduction from baseline in the percentage of days with urgency per week for ≥2 of the first 4 weeks post-treatment
  - Additional thresholds of percentage reduction from baseline were also evaluated (≥40% to ≥90%)
- Analyses were conducted using last observation carried forward methodology throughout the 10-week post-treatment period

RESULTS

- 3837 patients with IBS-D were included (rifaximin, n=3203; placebo, n=634), and the baseline average number of days per week with BM urgency was similar between the 2 groups (Table 2)

Table 2. Demographics and Baseline Characteristics

Parameter	Rifaximin (n=3203)	Placebo (n=634)
Age, y		
Mean (SD)	46.3 (13.8)	45.9 (14.6)
Range	18-88	18-82
Female, n (%)	2222 (69.4)	447 (70.5)
Race, n (%)		
White	2718 (84.9)	582 (91.8)
Black	334 (10.4)	44 (6.9)
Other	151 (4.7)	8 (1.3)
BM urgency number of days per week		
Mean (SD)	5.8 (1.7)	5.8 (1.6)
Range	0-7	0-7

BM = bowel movement; SD = standard deviation.

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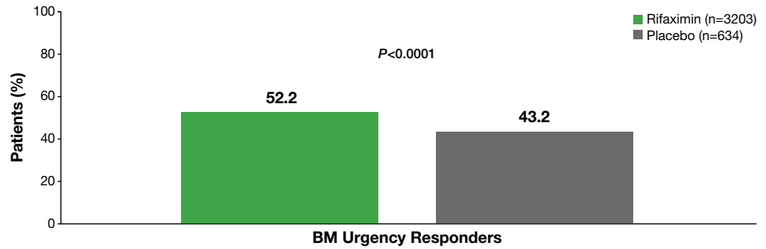
RESULTS

- A significantly greater percentage of patients treated with rifaximin were BM urgency responders versus those treated with placebo ($P<0.0001$; Figure 1)

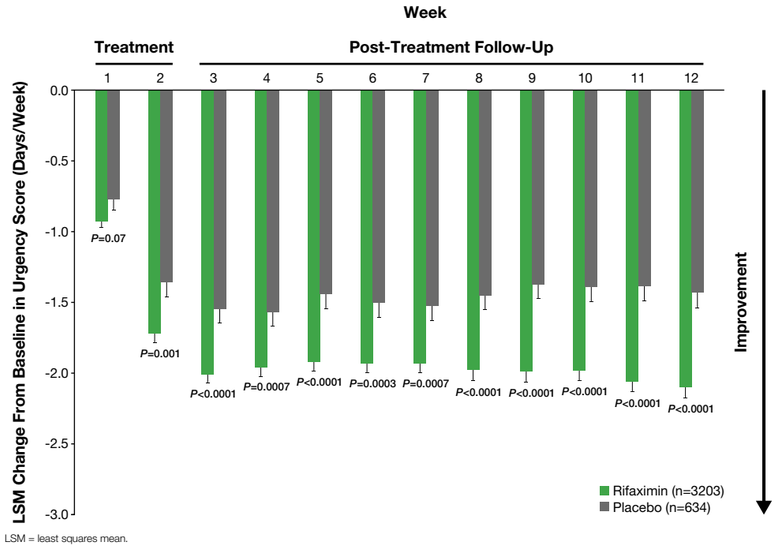
Figure 1. Bowel Movement Urgency Responders*



*Percentage of patients with ≥30% reduction from baseline in the percentage of days with BM urgency per week for ≥2 of the first 4 weeks post-treatment.
BM = bowel movement.

- Least-squares mean difference from baseline in BM urgency (days in a week) significantly favored rifaximin versus placebo during each week of the 10-week post-treatment period ($P \leq 0.0007$ vs placebo for each week; Figure 2)

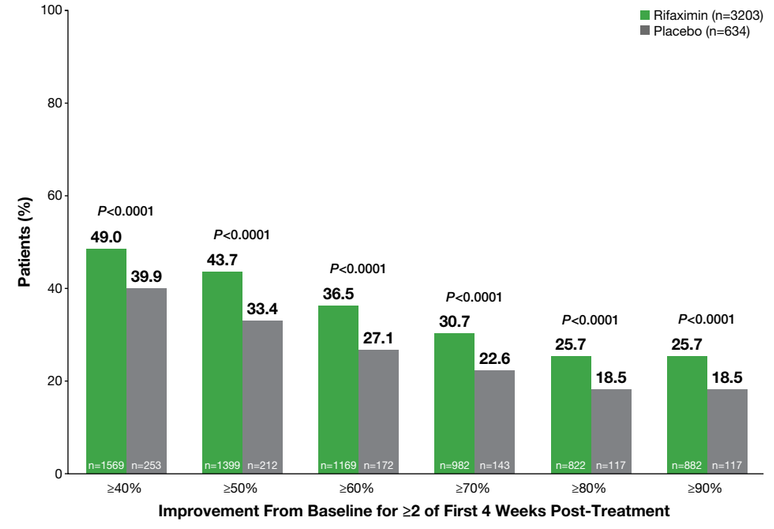
Figure 2. Change From Baseline in Bowel Movement Urgency, by Week



LSM = least squares mean.

- Using more stringent cutoffs for improvement, significantly more patients in the rifaximin group compared with the placebo group had ≥40%, ≥50%, ≥60% ≥70%, ≥80%, or ≥90% reductions from baseline in the percentage of days with BM urgency in a week for ≥2 of the first 4 weeks post-treatment (Figure 3)

Figure 3. Bowel Movement Urgency Responders, by Threshold for Improvement



CONCLUSIONS

- **A 2-week course of rifaximin 550 mg TID significantly improves BM urgency versus placebo in adults with IBS-D**

REFERENCES: **1.** Xifaxan® (rifaximin) tablets, for oral use [package insert]. Bridgewater, NJ: Salix Pharmaceuticals; 2020. **2.** Pimentel M, et al. *N Engl J Med*. 2011;364(1):22-32. **3.** Lembo A, et al. *Gastroenterology*. 2016;151(6):1113-1121. **4.** Lacy BE, et al. *Gastroenterology*. 2016;150(6):1393-1407. **5.** Zhu L, et al. *Health Qual Life Outcomes*. 2015;13:49. **6.** Wilson S, et al. *Br J Gen Pract*. 2004;54(504):495-502. **7.** Schoenfeld P, et al. *Aliment Pharmacol Ther*. 2014;39(10):1161-1168.

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